```
     FILE 'CAPLUS' ENTERED AT 14:08:12 ON 20 JUN 2003
L3             7 S (HISTAMINE OR IMIDAZOLE 4 ETHYLAMINE OR ERAMIN OR IMIDAZOL 4

=> d que
L3             7 SEA FILE=CAPLUS (HISTAMINE OR IMIDAZOLE 4 ETHYLAMINE OR ERAMIN
                 OR IMIDAZOL 4 YL ETHYL AMINO) (5A) (BENZENESULFONAMIDE# OR
                 SULFAMIDE# OR SULFONYLAMIDO OR SULFONYL AMIDO OR AMINO
                 SULFONLYL OR SULFONYL AMINO)


=>
```

=> d 1-7 bib ab

L3 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2002:736933 CAPLUS
DN 137:247603
TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as histamine-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, narcolepsy, and obesity
IN Bennani, Youssef L.; Faghih, Ramin; Dwight, Wesley J.; Vasudevan, Anil; Conner, Scott E.
PA USA
SO U.S. Pat. Appl. Publ., 62 pp., Cont.-in-part of U.S. Ser. No. 902,925.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002137931	A1	20020926	US 2002-44471	20020111
	US 2002035103	A1	20020321	US 2001-902925	20010711
	US 6515013	B2	20030204		
PRAI	US 2000-218084P	P	20000713		
	US 2001-902925	A2	20010711		

OS MARPAT 137:247603
AB Title compds. I [wherein Z = a bond or CH2; R1 = OR2, NR3R4, or 3-R5-4-R6-2,5-dioxoimidazolidinyl; R2 = H, alkoxycarbonyl, alkyl(carbonyl), aminocarbonyl, sulfono, or phosphono; R3 and R4 = independently H, alkenyl(sulfonyl), alkenyl(oxy)carbonyl, alkoxycarbonyl, alkyl(sulfonyl), alkylcarbonyl, aminocarbonyl, aminosulfonyl, alkynyl(sulfonyl), alkynyl(oxy)carbonyl, (un)substituted (hetero)arylalkyl, or (hetero)arylalkenylcarbonyl, etc.; R5, R6, and R7 = independently H or alkyl; or R1 and R7 together form =O; R8 = (cyclo)alkylcarbonyl, (un)substituted aryl(carbonyl), arylcarbonylaryl, arylcarbonylheterocyclyl, cycloalkylcarbonylaryl, cycloalkylcarbonylheterocyclyl, heterocyclyl(carbonyl), heterocyclylcarbonylaryl, or heterocyclylcarbonylheterocyclyl; R9 = H or alkyl; RA, RB, RC, and RD = independently H, alkenyl, alkoxy(alkoxy), (alkoxy)alkyl, alkoxycarbonyl, alkylcarbonyl(oxy), alkylsulfinyl, alkylsulfonyl, alkylthio, alkynyl, amino(alkyl), aminocarbonyl, (carboxy)alkyl, (cyano)alkyl, formyl, halo(alkoxy), haloalkyl, (hydroxy)alkyl, SH, or NO2, etc.; and pharmaceutically acceptable salts] were prepd. as histamine-3 receptor ligands. For example, 4'-[3-[(3R)-3-aminopyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile in CH2Cl2 was treated with polymer supported N,N-diisopropylethylamine, catalytic amt. of DMAP, and 4-methoxybenzenesulfonyl chloride. After shaking at ambient temp. for 14 h, the mixt. was treated with tris(2-aminoethyl)amine-polystyrene resin and the mixt. shaken for an addnl. 2 h to give the [[(biphenylyloxy)propyl]pyrrolidinyl]benzenesulfonamide II (79%). The latter bound to the histamine-3 receptor with Ki of 12 nM. I are useful for the treatment of acute myocardial infarction, asthma, bipolar disorder, cognitive enhancement, cutaneous carcinoma, depression, gastrointestinal disorders, inflammation, jet lag, medullary thyroid carcinoma, melanoma, Meniere's disease, migraine, motion sickness, obesity, pain, Parkinson's disease, schizophrenia, seizures, septic shock, Tourette's syndrome, Vertigo, wakefulness, Alzheimer's disease, attention-deficit hyperactivity disorder (ADHD), epilepsy, and narcolepsy (no data).

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2002:221215 CAPLUS
DN 136:263087
TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as histamine-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy

IN Bennani, Youssef L.; Faghih, Ramin; Dwight, Wesley J.; Vasudevan, Anil; Conner, Scott E.
PA USA
SO U.S. Pat. Appl. Publ., 54 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002035103	A1	20020321	US 2001-902925	20010711
	US 6515013	B2	20030204		
	US 2002137931	A1	20020926	US 2002-44471	20020111
PRAI	US 2000-218084P	P	20000713		
	US 2001-902925	A2	20010711		

OS MARPAT 136:263087
AB Title compds. I [wherein Z = a bond or CH2; R1 = OR2, NR3R4, or substituted 2,5-dioxoimidazolidinyl; R2 = H, alkoxycarbonyl, alkyl(carbonyl), aminocarbonyl, sulfono, or phosphono; R3 and R4 = independently H, alkenyl(sulfonyl), alkenyl(oxy)carbonyl, alkoxycarbonyl, alkyl(sulfonyl), alkylcarbonyl, aminocarbonyl, aminosulfonyl, alkynyl(sulfonyl), alkynyl(oxy)carbonyl, or (un)substituted (hetero)arylalkyl, (hetero)arylalkenylcarbonyl, etc.; R7 = H or alkyl; or R1 and R7 together form :O; R8 = (cyclo)alkylcarbonyl, or (un)substituted aryl(carbonyl), arylcarbonylaryl, arylcarbonylheterocyclyl, cycloalkylcarbonylaryl, cycloalkylcarbonylheterocyclyl, heterocyclyl(carbonyl), heterocyclylcarbonylaryl, or heterocyclylcarbonylheterocyclyl; R9 = H or alkyl] were prepd. as histamine-3 receptor ligands. For example, 4'-[3-[(3R)-3-aminopyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile in CH2Cl2 was treated with polymer supported N,N-diisopropylethylamine, catalytic N,N-dimethylaminopyridine, and 4-methoxybenzenesulfonyl chloride. After shaking at ambient temp. for 14 h, the mixt. was treated with tris(2-aminoethyl)amine-polystyrene resin and the mixt. shaken for an addnl. 2 h to give the [[(biphenylyloxy)propyl]pyrrolidinyl]benzenesulfonamide II (79%). The latter bound to the histamine-3 receptor with Ki of 12 nM. I are useful for the treatment of acute myocardial infarction, asthma, cutaneous carcinoma, depression, inflammation, medullary thyroid carcinoma, melanoma, Meniere's disease, migraine, motion sickness, obesity, pain, Parkinson's disease, schizophrenia, seizures, septic shock, Alzheimer's disease, attention-deficit hyperactivity disorder (ADHD), epilepsy, and narcolepsy.

L3 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 1999:737587 CAPLUS
DN 132:87751
TI 4-Chlorobenzyl sulfonamide and **sulfamide** derivatives of **histamine** homologues: the design of potent histamine H3 receptor antagonists
AU Tozer, Matthew J.; Buck, Ildiko M.; Cooke, Tracey; Kalindjian, S. Barret; McDonald, Iain M.; Pether, Michael J.; Steel, Katherine I. M.
CS The James Black Foundation, London, SE24 9JE, UK
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(21), 3103-3108
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB 4-Chlorophenylmethanesulfonamide and (4-chlorobenzyl)**sulfamide** derivs. of **histamine** homologues were prepd. and found to be potent and selective histamine H3 receptor antagonists. High receptor affinity and low differences in the data from the bioassays were achieved with the imidazol-4-ylbutyl analogs.
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 1999:504279 CAPLUS
DN 131:286325
TI Novel carbonic anhydrase isozymes I, II and IV activators incorporating sulfonyl-histamino moieties
AU Briganti, Fabrizio; Scozzafava, Andrea; Supuran, Claudiu T.
CS Universita degli Studi, Laboratorio di Chimica Inorganica e Bioinorganica, Florence, 50121, Italy
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(14), 2043-2048
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB **Sulfonylamido**(ureido) derivs. of **histamine** were synthesized by an original procedure in order to obtain tight-binding activators of the zinc enzyme carbonic anhydrase (CA), exploiting the binding energy of the alkyl/arylsulfonyl moieties with amino acid residues at the entrance of the active site. In contrast to the lead mol., histamine, the new derivs. possessed higher affinity for three different CA isoenzymes, as evidenced by comparing the affinity consts. of these compds. for isoenzyme CA II.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 1998:606886 CAPLUS
DN 129:290093
TI Novel H3 receptor antagonists. Sulfonamide homologs of histamine
AU Wolin, Ronald; Connolly, Michael; Afonso, Adriano; Hey, John A.; She, Hoyan; Rivelli, Maria A.; Willams, Shirley M.; West, Robert E., Jr.
CS Department of Chemistry, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SO Bioorganic & Medicinal Chemistry Letters (1998), 8(16), 2157-2162
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 129:290093
AB Sulfonamides derived from 4(5)-(.omega.-aminoalkyl)-1H-imidazoles contg. chain lengths of three- to five-carbons were synthesized. Good to moderate H3 receptor binding affinities were obsd. for several Bu and pentyl homologs, whereas binding affinities were considerably weaker in the Pr series. Sepn. of the imidazole ring and the sulfonamide unit by a four- or five-carbon tether afforded potent H3 receptor antagonists.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

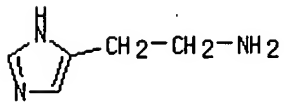
L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 1982:193208 CAPLUS
DN 96:193208
TI Comparison of airway obstruction induced by propranolol and YM-09538 (a combined .alpha.- and .beta.-adrenoceptor blocking drug)
AU Tomioka, K.; Yamada, T.; Takenaka, T.
CS Cent. Res. Lab., Yamanouchi Pharm. Co. Ltd., Tokyo, 174, Japan
SO Archives Internationales de Pharmacodynamie et de Therapie (1982), 256(1), 97-107
CODEN: AIPTAK; ISSN: 0003-9780
DT Journal
LA English
AB In the isolated guinea-pig right atria and tracheal strips, both dl-propranolol (I) [13013-17-7] and YM-09538 (II) [70958-86-0] caused a parallel shift of the dose-response curve for isoproterenol to the right, indicating that these 2 drugs block nonselectively the .beta.1- and

.beta.2-adrenoceptors. Propranolol potentiated the histamine [51-45-6]-induced bronchoconstriction in the anesthetized dogs, whereas YM-09538 did not affect the histamine-induced bronchoconstriction. Propranolol degranulated the isolated rat mesenteric mast cells in contrast to YM-09538 which had no significant effect on mast cells. Neither propranolol nor YM-09538 affected the hapten-specific IgE antibody response in female BDF1 mice. Apparently, YM-09538 has a much lesser effect on airway function than propranolol.

L3 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 1964:63800 CAPLUS
DN 60:63800
OREF 60:11257e
TI Ways of overcoming insulin resistance in patients with diabetes mellitus
AU Kamysheva, E. P.
SO Vopr. Neiroendokrinol. Patol., Gorki, Sb. (1963) 254-7
From: Ref. Zh., Biol. Khim. 1963, Abstr. No. 22F-1353.
DT Journal
LA Unavailable
AB Administration of hyaluronidase, **histamine**, hexonium, and **sulfamide** prepns. and needle pricking were effective in overcoming resistance to insulin in diabetics.

=>

RN 51-45-6 REGISTRY
CN 1H-Imidazole-4-ethanamine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Histamine (8CI)
OTHER NAMES:
CN β-Imidazolyl-4-ethylamine
CN 2-(1H-Imidazol-4-yl)ethanamine
CN 2-(1H-Imidazol-4-yl)ethylamine
CN 2-(1H-Imidazol-5-yl)ethylamine
CN 2-(4-Imidazolyl)ethanamine
CN 2-(4-Imidazolyl)ethylamine
CN 4-(2-Aminoethyl)imidazole
CN 5-Imidazoleethylamine
CN Eramin
CN Ergamine
CN Ergotidine
CN Imidazole-4-ethylamine
FS 3D CONCORD
MF C5 H9 N3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

31050 REFERENCES IN FILE CA (1957 TO DATE)
386 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
31060 REFERENCES IN FILE CAPLUS (1957 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 43	Jun 06	PASCAL enhanced with additional data

NEWS EXPRESS	April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 06:05:56 ON 20 JUN 2003

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 06:06:21 ON 20 JUN 2003
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FILE COVERS 1907 - 20 Jun 2003 VOL 138 ISS 26
FILE LAST UPDATED: 19 Jun 2003 (20030619/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> e dementia/ct

E#	FREQUENCY	AT		TERM
E1	0	2		DEMBER PHOTOVOLTAIC EFFECT/CT
E2	0	2		DEMECOLCINE/CT
E3	0	2	-->	DEMENTIA/CT
E4	0	2		DEMENTIA MENTAL DISORDER/CT
E5	0	2		DEMENTIA PRAECOX/CT
E6	0	2		DEMENTIA WITH LEWY BODIES/CT
E7	0	1		DEMERARAE/CT
E8	0	1		DEMERARANUM/CT
E9	194	2		DEMERCURATION/CT
E10	10	3		DEMERCURATION CATALYSTS/CT
E11	1			DEMEREC/CT
E12	1			DEMEREC, MILISLAV/CT

```
=> e e3+/ct
'+' IS NOT VALID HERE
For an explanation of the EXPAND command, enter "HELP EXPAND" at an
arrow prompt (=>).

=> d e3+/ct
'E3+' MUST END IN '/Q', '/A', '/L', '/S' OR '/B'
The saved name for a query (or structure or screen set) must end with
'/Q'.  The saved name for an answer set must end with '/A'.  The saved
name for an L# list must end with '/L'.  SDI request names must end
with '/S'.  To see a list of all saved query, answer set,, and L# list
names for this loginid, enter "DISPLAY SAVED" at an arrow
prompt (=>).  Enter "DISPLAY SAVED/S" to see a list of SDI request
names.  Enter "DISPLAY SAVED/B" to see a list of BATCH search
requests.

=> file caplus wpids medline embase
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               0.83       1.04

FILE 'CAPLUS' ENTERED AT 06:07:28 ON 20 JUN 2003
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FILE 'WPIDS' ENTERED AT 06:07:28 ON 20 JUN 2003
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FILE 'MEDLINE' ENTERED AT 06:07:28 ON 20 JUN 2003

FILE 'EMBASE' ENTERED AT 06:07:28 ON 20 JUN 2003
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=> s dementia or alzheimer?
L1       172320 DEMENTIA OR ALZHEIMER?

=> s l1 or neurodegenerat? disease#
L2       182615 L1 OR NEURODEGENERAT? DISEASE#

=> s ((sulfonylamido or sulfonyl amido) (2a) histamine) or nsaid or non steroidal (a
MISSING OPERATOR 'STEROIDAL (ANTIINFLAM'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s ((sulfonylamido or sulfonyl amido) (2a) histamine) or nsaid or ((non steroidal
UNMATCHED RIGHT PARENTHESIS 'ESTROGEN)'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s ((sulfonylamido or sulfonyl amido) (2a) histamine) or nsaid or ((non steroidal

 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS, WPIDS, MEDLINE, EMBASE'
AT 06:15:49 ON 20 JUN 2003
FILE 'CAPLUS' ENTERED AT 06:15:49 ON 20 JUN 2003
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
FILE 'WPIDS' ENTERED AT 06:15:49 ON 20 JUN 2003
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FILE 'MEDLINE' ENTERED AT 06:15:49 ON 20 JUN 2003
FILE 'EMBASE' ENTERED AT 06:15:49 ON 20 JUN 2003
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    60.51      61.55

=> d his

     (FILE 'HOME' ENTERED AT 06:05:56 ON 20 JUN 2003)

     FILE 'CAPLUS' ENTERED AT 06:06:21 ON 20 JUN 2003
               E DEMENTIA/CT

     FILE 'CAPLUS, WPIDS, MEDLINE, EMBASE' ENTERED AT 06:07:28 ON 20 JUN 2003
L1       172320 S DEMENTIA OR ALZHEIMER?
L2       182615 S L1 OR NEURODEGENERAT? DISEASE#
L3      1127914 S ((SULFONYLAMIDO OR SULFONYL AMIDO) (2A) HISTAMINE) OR NSAID O

=> s l2 (l) l3
L4         3550 L2 (L) L3

=> s l4 and ((sulfonylamido (5a) histamine) or (sulfonyl (5a) amido (5a) histamine))
L5            0 L4 AND ((SULFONYLAMIDO (5A) HISTAMINE) OR (SULFONYL (5A) AMIDO
                (5A) HISTAMINE))

=> s l4 and histamine
L6           24 L4 AND HISTAMINE

=> s l2 and histamine
L7          496 L2 AND HISTAMINE

=> s l7 and (histamine (10a) sulfonyl)
L8            3 L7 AND (HISTAMINE (10A) SULFONYL)

=> d 1-3 bib hit

L8   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2003 ACS
```

Full Text | Citing References

```
AN   2002:781497  CAPLUS
DN   137:262957
TI   Preparation of aryloxyalkylamines as histamine H3 receptor modulators
IN   Schwartz, Jean-Charles; Arrang, Jean-Michel; Garbarg, Monique; Lecomte,
     Jeanne-Marie; Ligneau, Xavier; Schunack, Walter G.; Stark, Holger;
     Ganellin, Charon Robin; Leurquin, Fabien; Sigurd, Elz
PA   Societe Civile Bioprojet, Fr.
SO   PCT Int. Appl., 195 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
     ---------------     ----  --------      ---------------  --------
PI   WO 2000006254       A2    20000210      WO 1999-EP5744   19990729
     WO 2000006254       A3    20000504
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
             JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
             MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
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TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 978512	A1	20000209	EP 1998-401944	19980729	
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EP 982300	A2	20000301	EP 1998-403351	19981231	
EP 982300	A3	20000308			
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AU 9955119	A1	20000221	AU 1999-55119	19990729	
EP 1100503	A2	20010523	EP 1999-941543	19990729	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002521463	T2	20020716	JP 2000-562103	19990729	
PRAI EP 1998-401944	A	19980729			
EP 1998-403351	A	19981231			
WO 1999-EP5744	W	19990729			

OS MARPAT 137:262957

TI Preparation of aryloxyalkylamines as **histamine** H3 receptor modulators

AB The title non-imidazole compds. I [wherein n = 2-8; m = 0-5; X = O, S; R1, R2 = alkyl, cycloalkyl; NR1R2 = (unsatd.) N-contg. ring, substituted piperazino; R3 = halo, alkyl, cycloalkyl, CF3, aryl, alkoxy, aryloxy, NO2, CHO, alkanoyl, aroyl, aralkanoyl, amino, carboxamido, cyano, alkoximino, alkenyl, alkynyl, etc.; and their pharmaceutically acceptable salts, hydrates, polymorphic cryst. structures,optical isomers, racemates, diastereoisomers, and enantiomers] were prepd. as antagonists and/or agonists of the **histamine** H3-receptors. Thus, 1-[3-(4-cyanophenoxy)prg167opyl]piperidine hydrogen oxalate (general prepn. given) increased telemethylhistamine in mice with ED50 = 0.20 mg/kg orally. I are useful for the treatment of central nervous system disorders, in particular **Alzheimer**'s disease, mood and attention alterations, cognitive deficits in psychiatric pathologies, obesity, vertigo, and motion sickness (no data).

ST aryloxyalkylamine prepn **histamine** receptor antagonist agonist; azaheterocycloalkoxybenzene nonimidazole prepn **histamine** receptor antagonist agonist; nootropic aryloxyalkylamine; antiobesity agent aryloxyalkylamine; pyschotropic aryloxyalkylamine; memory enhancer aryloxyalkylamine; motion sickness treatment aryloxyalkylamine

IT Intestine, disease
(Crohn's; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Antihistamines
(H3; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Mental disorder
(attention deficit disorder; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Mental activity
(attention, stimulators; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Bronchi
(bronchitis; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Eye, disease
(conjunctivitis; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Bladder
(cystitis; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Mental disorder
(depression; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Urogenital tract
(diseases, inflammation; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Intestine, disease
(duodenum, ulcer; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Uterus, disease
(endometritis; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Digestive tract
(gastroenteritis; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Bladder
Defecation
(incontinence; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Heart, disease
(infarction, therapeutic agents; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Heart, disease
(infarction; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Eye, disease
Respiratory tract
(inflammation; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Intestine, disease
(irritable bowel syndrome; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Headache
(migraine; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Mental disorder
(mood-affecting; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Ovarian cycle
(premenstrual syndrome; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)
IT Allergy inhibitors
Alzheimer's disease
Analgesics
Anti-**Alzheimer**'s agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidepressants
Antimigraine agents
Antiobesity agents
Antiulcer agents
Anxiolytics
Arthritis
Asthma
Cognition enhancers
Dermatitis

Dizziness
Heart, disease
Human
Hypnotics and Sedatives
Nervous system agents
Pruritus
Psychotropics
Stress, animal
Urticaria
(prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Nose
(rhinitis; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Memory, biological
(stimulators; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Bronchi
Trachea (anatomical)
(tracheobronchitis; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Motion sickness
(treatment; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Stomach, disease
(ulcer; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT Intestine, disease
(ulcerative colitis; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT 23999-21-5P, 1-Propanamine, N,N-diethyl-3-(4-nitrophenoxy)- 27078-39-3P 46843-28-1P, Benzonitrile, 4-[3-(diethylamino)propoxy]- 46926-57-2P, Benzonitrile, 4-[4-(diethylamino)butoxy]- 49773-11-7P, Benzonitrile, 4-[2-(diethylamino)ethoxy]- 70403-69-9P, 5-Piperidinopentylamine 77427-42-0P 82625-46-5P, Benzaldehyde, 4-[3-(1-piperidinyl)propoxy]- 86355-72-8P, Piperidine, 1-(5-phenoxypentyl)- 92322-18-4P, Pyrrolidine, 1-(4-phenoxybutyl)- 92374-75-9P, 1-[3-(4-Nitrophenoxy)propyl]piperidine 93699-55-9P, 1-Propanone, 1-[4-[3-(diethylamino)propoxy]phenyl]- 99759-00-9P 116871-18-2P, Pyrrolidine, 1-(3-phenoxypropyl)- 146440-15-5P, Benzonitrile, 4-[3-(dimethylamino)propoxy]- 146440-20-2P, Benzonitrile, 4-[3-(1-piperidinyl)propoxy]- 164029-23-6P, Benzonitrile, 4-[[5-(1-piperidinyl)pentyl]oxy]- 169815-42-3P, 7-Chloro-4-(3-piperidinopropylamino)quinoline 172018-41-6P 199920-60-0P 220727-93-5P, 1-Pentanamine, N-ethyl-N-methyl-5-phenoxy- 220727-94-6P, 1-Pentanamine, N-ethyl-N-methyl-5-phenoxy-, ethanedioate (1:1) 220727-95-7P, 1-Pentanamine, N-ethyl-5-phenoxy-N-propyl- 220727-96-8P, 1-Pentanamine, N-ethyl-5-phenoxy-N-propyl-, ethanedioate (1:1) 220727-99-1P, Pyrrolidine, 1-(5-phenoxypentyl)- 220728-00-7P, Pyrrolidine, 1-(5-phenoxypentyl)-, ethanedioate (1:1) 220728-01-8P, Piperidine, 1-(5-phenoxypentyl)-, ethanedioate (1:1) 220728-02-9P, 1H-Azepine, hexahydro-1-(5-phenoxypentyl)- 220728-03-0P, 1H-Azepine, hexahydro-1-(5-phenoxypentyl)-, ethanedioate (1:1) 220728-04-1P, Morpholine, 4-(5-phenoxypentyl)- 220728-05-2P, Morpholine, 4-(5-phenoxypentyl)-, ethanedioate (1:1) 220728-07-4P, Pyrrolidine, 1-[5-(4-fluorophenoxy)pentyl]- 220728-08-5P, Pyrrolidine, 1-[5-(4-fluorophenoxy)pentyl]-, ethanedioate (1:1) 220728-09-6P, Pyrrolidine, 1-[5-(4-chlorophenoxy)pentyl]- 220728-10-9P, Pyrrolidine, 1-[5-(4-chlorophenoxy)pentyl]-, ethanedioate (1:1) 220728-11-0P, Pyrrolidine, 1-[5-(3-chlorophenoxy)pentyl]- 220728-12-1P, Pyrrolidine, 1-[5-(3-chlorophenoxy)pentyl]-, ethanedioate (1:1) 220728-13-2P,

Benzenamine, 4-[[5-(1-pyrrolidinyl)pentyl]oxy]- 220728-15-4P, Pyrrolidine, 1-[5-(4-methylphenoxy)pentyl]- 220728-16-5P, Pyrrolidine, 1-[5-(4-methylphenoxy)pentyl]-, ethanedioate (1:1) 220728-17-6P, Pyrrolidine, 1-[5-(4-nitrophenoxy)pentyl]- 220728-18-7P, Pyrrolidine, 1-[5-(4-nitrophenoxy)pentyl]-, ethanedioate (1:1) 220728-19-8P, Pyrrolidine, 1-[5-(3-nitrophenoxy)pentyl]- 220728-20-1P, Pyrrolidine, 1-[5-(3-nitrophenoxy)pentyl]-, ethanedioate (1:1) 220728-21-2P, Benzonitrile, 4-[[5-(1-pyrrolidinyl)pentyl]oxy]- 220728-23-4P, Benzonitrile, 3-[[5-(1-pyrrolidinyl)pentyl]oxy]- 220728-24-5P, Benzonitrile, 3-[[5-(1-pyrrolidinyl)pentyl]oxy]-, ethanedioate (1:1) 256952-10-0P, Piperidine, 2-methyl-1-(5-phenoxypentyl)- 256952-11-1P, Piperidine, 1-(5-phenoxypentyl)-4-propyl- 256952-12-2P, Piperidine, 4-methyl-1-(5-phenoxypentyl)- 256952-13-3P, Piperidine, 3-methyl-1-(5-phenoxypentyl)- 256952-14-4P, Piperazine, 1-acetyl-4-(5-phenoxypentyl)- 256952-15-5P, Piperidine, 3,5-dimethyl-1-(5-phenoxypentyl)-, (3R,5R)-rel- 256952-16-6P, Piperidine, 3,5-dimethyl-1-(5-phenoxypentyl)-, (3R,5S)-rel- 256952-17-7P, Piperidine, 2,6-dimethyl-1-(5-phenoxypentyl)-, (2R,6S)-rel- 256952-18-8P, 4-Piperidinecarboxylic acid, 1-(5-phenoxypentyl)-, ethyl ester 256952-19-9P, 3-Piperidinecarboxylic acid, 1-(5-phenoxypentyl)-, ethyl ester 256952-20-2P, Pyridine, 1,2,3,6-tetrahydro-1-(5-phenoxypentyl)- 256952-21-3P, Pyrrolidine, 1-[5-(4-methoxyphenoxy)pentyl]- 256952-22-4P, Pyrrolidine, 1-[5-(2-naphthalenyloxy)pentyl]- 256952-23-5P, Pyrrolidine, 1-[5-(1-naphthalenyloxy)pentyl]- 256952-24-6P, Pyrrolidine, 1-[5-([1,1'-biphenyl]-4-yloxy)pentyl]- 256952-25-7P, Pyrrolidine, 1-[5-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]pentyl]- 256952-26-8P, Pyrrolidine, 1-[5-([1,1'-biphenyl]-3-yloxy)pentyl]- 256952-27-9P, 1H-Pyrrole, 2,5-dihydro-1-(5-phenoxypentyl)- 256952-28-0P, Pyrrolidine, 1-[5-[(5,6,7,8-tetrahydro-1-naphthalenyl)oxy]pentyl]- 256952-29-1P, Pyrrolidine, 1-(6-phenoxyhexyl)- 256952-30-4P, Piperidine, 3-methyl-1-[5-(4-nitrophenoxy)pentyl]- 256952-31-5P, Ethanone, 1-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]- 256952-32-6P, Methanone, phenyl[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]- 256952-34-8P, Ethanone, 2-phenyl-1-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]- 256952-36-0P, Acetamide, N-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]- 256952-38-2P, Pyrrolidine, 1-[5-(4-phenoxyphenoxy)pentyl]- 256952-41-7P, Benzamide, N-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]- 256952-43-9P, Benzenemethanol, α-methyl-4-[[5-(1-pyrrolidinyl)pentyl]oxy]- 256952-44-0P, Benzonitrile, 4-[[5-(diethylamino)pentyl]oxy]- 256952-45-1P, Benzonitrile, 4-[[5-(dimethylamino)pentyl]oxy]- 256952-46-2P, Benzonitrile, 4-[[5-(dipropylamino)pentyl]oxy]- 256952-48-4P, Benzonitrile, 4-[3-(1-pyrrolidinyl)propoxy]- 256952-49-5P, Benzonitrile, 4-[3-(hexahydro-1H-azepin-1-yl)propoxy]- 256952-51-9P, Benzonitrile, 4-[[6-(diethylamino)hexyl]oxy]- 256952-54-2P, Benzonitrile, 4-[3-(dipropylamino)propoxy]- 256952-57-5P, Benzenemethanol, 4-[3-(diethylamino)propoxy]-α-methyl- 256952-61-1P, Ethanone, 1-[4-[3-(diethylamino)propoxy]phenyl]-, oxime 256952-65-5P, Ethanone, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]- 256952-69-9P, Ethanone, 1-[4-[3-(3-methyl-1-piperidinyl)propoxy]phenyl]- 256952-72-4P, Ethanone, 1-[4-[3-[(3R,5R)-3,5-dimethyl-1-piperidinyl]propoxy]phenyl]-, rel- 256952-76-8P, Ethanone, 1-[4-[3-(4-methyl-1-piperidinyl)propoxy]phenyl]- 256952-78-0P, 1-Propanone, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]- 256952-81-5P, Ethanone, 1-[4-[3-[(3R,5S)-3,5-dimethyl-1-piperidinyl]propoxy]phenyl]-, rel- 256952-84-8P, 1-Propanone, 2-methyl-1-[4-[3-(1-piperidinyl)propoxy]phenyl]- 256952-87-1P, 1-Butanone, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]- 256952-89-3P, Ethanone, 1-[4-[3-(3,6-dihydro-1(2H)-pyridinyl)propoxy]phenyl]- 256952-94-0P, Pyrrolidine, 1-[5-(phenylthio)pentyl]- 256952-95-1P, Pyrrolidine,

1-[4-(phenylthio)butyl]- 256952-96-2P, Ethanone, 1-[4-[3-(diethylamino)propoxy]phenyl]- 256953-01-2P, Piperidine, 2-methyl-1-(5-phenoxypentyl)-, ethanedioate (10:11) 256953-02-3P, Piperidine, 1-(5-phenoxypentyl)-4-propyl-, ethanedioate (1:1) 256953-03-4P, Piperidine, 4-methyl-1-(5-phenoxypentyl)-, ethanedioate (1:1) 256953-04-5P, Piperidine, 3-methyl-1-(5-phenoxypentyl)-, ethanedioate (1:1) 256953-05-6P, Piperazine, 1-acetyl-4-(5-phenoxypentyl)-, ethanedioate (1:1) 256953-06-7P, Piperidine, 3,5-dimethyl-1-(5-phenoxypentyl)-, (3R,5R)-rel-, ethanedioate (1:1) 256953-07-8P, Piperidine, 3,5-dimethyl-1-(5-phenoxypentyl)-, (3R,5S)-rel-, ethanedioate (1:1) 256953-08-9P, Piperidine, 2,6-dimethyl-1-(5-phenoxypentyl)-, hydrochloride, (2R,6S)-rel- 256953-09-0P, 4-Piperidinecarboxylic acid, 1-(5-phenoxypentyl)-, ethyl ester, ethanedioate (1:1) 256953-10-3P, 3-Piperidinecarboxylic acid, 1-(5-phenoxypentyl)-, ethyl ester, ethanedioate (1:1) 256953-11-4P, Pyridine, 1,2,3,6-tetrahydro-1-(5-phenoxypentyl)-, ethanedioate (1:1) 256953-12-5P, Pyrrolidine, 1-[5-(4-methoxyphenoxy)pentyl]-, ethanedioate (1:1) 256953-13-6P, Benzonitrile, 4-[[5-(1-pyrrolidinyl)pentyl]oxy]-, ethanedioate (10:11) 256953-14-7P, Pyrrolidine, 1-[5-(2-naphthalenyloxy)pentyl]-, ethanedioate (1:1) 256953-15-8P, Pyrrolidine, 1-[5-(1-naphthalenyloxy)pentyl]-, ethanedioate (4:5) 256953-16-9P, Pyrrolidine, 1-[5-([1,1'-biphenyl]-4-yloxy)pentyl]-, ethanedioate (1:1) 256953-17-0P, Pyrrolidine, 1-[5-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]pentyl]-, ethanedioate (1:1) 256953-18-1P, Pyrrolidine, 1-[5-([1,1'-biphenyl]-3-yloxy)pentyl]-, ethanedioate (10:11) 256953-19-2P, 1H-Pyrrole, 2,5-dihydro-1-(5-phenoxypentyl)-, ethanedioate (1:1) 256953-20-5P, Pyrrolidine, 1-[5-[(5,6,7,8-tetrahydro-1-naphthalenyl)oxy]pentyl]-, ethanedioate (1:1) 256953-21-6P, Pyrrolidine, 1-(4-phenoxybutyl)-, ethanedioate (1:1) 256953-22-7P, Pyrrolidine, 1-(6-phenoxyhexyl)-, ethanedioate (10:11) 256953-23-8P, Pyrrolidine, 1-[5-(phenylthio)pentyl]-, ethanedioate (10:11) 256953-24-9P, Pyrrolidine, 1-[4-(phenylthio)butyl]-, ethanedioate (1:1) 256953-25-0P, Pyrrolidine, 1-(3-phenoxypropyl)-, ethanedioate (1:1) 256953-26-1P, Piperidine, 3-methyl-1-[5-(4-nitrophenoxy)pentyl]-, ethanedioate (1:1) 256953-27-2P, Ethanone, 1-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]-, ethanedioate (1:1) 256953-28-3P, Benzenamine, 4-[[5-(1-pyrrolidinyl)pentyl]oxy]-, ethanedioate (10:21) 256953-29-4P, 1-Propanamine, N,N-diethyl-3-(4-nitrophenoxy)-, ethanedioate (1:1) 256953-30-7P, Benzonitrile, 4-[3-(diethylamino)propoxy]-, ethanedioate (1:1) 256953-31-8P, Methanone, phenyl[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]-, ethanedioate (1:1) 256953-32-9P, Ethanone, 2-phenyl-1-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]-, ethanedioate (1:1) 256953-33-0P, Ethanone, 1-[4-[3-(diethylamino)propoxy]phenyl]-, ethanedioate (10:11) 256953-34-1P, Acetamide, N-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]-, ethanedioate (1:1) 256953-35-2P, Pyrrolidine, 1-[5-(4-phenoxyphenoxy)pentyl]-, ethanedioate (1:1) 256953-36-3P, Benzamide, N-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]-, ethanedioate (10:11) 256953-37-4P, Benzenemethanol, α-methyl-4-[[5-(1-pyrrolidinyl)pentyl]oxy]-, ethanedioate (1:1) (salt) 256953-38-5P, Benzonitrile, 4-[[5-(diethylamino)pentyl]oxy]-, ethanedioate (1:1) 256953-39-6P, Benzonitrile, 4-[[5-(1-piperidinyl)pentyl]oxy]-, ethanedioate (1:1) 256953-40-9P, Benzonitrile, 4-[[5-(dimethylamino)pentyl]oxy]-, ethanedioate (1:1) 256953-41-0P, Benzonitrile, 4-[2-(diethylamino)ethoxy]-, ethanedioate (1:1) 256953-42-1P, Benzonitrile, 4-[3-(dimethylamino)propoxy]-, ethanedioate (1:1) 256953-43-2P, Benzonitrile, 4-[4-(diethylamino)butoxy]-, ethanedioate (1:1) 256953-44-3P, Benzonitrile, 4-[[5-(dipropylamino)pentyl]oxy]-, ethanedioate (1:1) 256953-45-4P, Benzonitrile, 4-[3-(1-pyrrolidinyl)propoxy]-, ethanedioate (10:11) 256953-46-5P, Benzonitrile,

4-[3-(1-piperidinyl)propoxy]-, ethanedioate (1:1) 256953-47-6P, Benzonitrile, 4-[3-(hexahydro-1H-azepin-1-yl)propoxy]-, ethanedioate (1:1) 256953-48-7P, Benzonitrile, 4-[[6-(diethylamino)hexyl]oxy]-, ethanedioate (1:1) 256953-49-8P, Benzonitrile, 4-[3-(dipropylamino)propoxy]-, ethanedioate (1:1) 256953-50-1P, Benzenemethanol, 4-[3-(diethylamino)propoxy]-α-methyl-, ethanedioate (1:1) (salt) 256953-51-2P, Ethanone, 1-[4-[3-(diethylamino)propoxy]phenyl]-, oxime, ethanedioate (1:1) 256953-52-3P, Ethanone, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]-, ethanedioate (1:1) 256953-53-4P, Ethanone, 1-[4-[3-(3-methyl-1-piperidinyl)propoxy]phenyl]-, ethanedioate (1:1) 256953-54-5P, Ethanone, 1-[4-[3-[(3R,5R)-3,5-dimethyl-1-piperidinyl]propoxy]phenyl]-, rel-, ethanedioate (1:1) 256953-55-6P, Ethanone, 1-[4-[3-(4-methyl-1-piperidinyl)propoxy]phenyl]-, ethanedioate (1:1) 256953-56-7P, 1-Propanone, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]-, ethanedioate (1:1) 256953-58-9P, Ethanone, 1-[4-[3-[(3R,5S)-3,5-dimethyl-1-piperidinyl]propoxy]phenyl]-, rel-, ethanedioate (1:1) 256953-59-0P, Benzaldehyde, 4-[3-(1-piperidinyl)propoxy]-, ethanedioate (1:1) 256953-60-3P, 1-Propanone, 2-methyl-1-[4-[3-(1-piperidinyl)propoxy]phenyl]-, ethanedioate (1:1) 256953-61-4P, 1-Propanone, 1-[4-[3-(diethylamino)propoxy]phenyl]-, ethanedioate (2:3) 256953-62-5P, 1-Butanone, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]-, ethanedioate (1:1) 256953-63-6P, Ethanone, 1-[4-[3-(3,6-dihydro-1(2H)-pyridinyl)propoxy]phenyl]-, ethanedioate (10:11) 362665-49-4P 362665-51-8P 362665-52-9P 362665-53-0P 362665-54-1P, 3-Phenylpropyl 3-piperidinopropyl ether 362665-55-2P 362665-56-3P, 3-(4-Chlorophenyl)propyl 3-piperidinopropyl ether 362665-57-4P 362665-58-5P, 1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]piperidine 362665-63-2P 362665-66-5P, N-(6-Phenylhexyl)piperidine 362665-67-6P, N-(6-Phenylhexyl)piperidine hydrogen oxalate 362665-74-5P, 3-(4-Chlorobenzyl)-5-(2-piperidinoethyl)-1,2,4-oxadiazole hydrogen oxalate 362665-81-4P, 3-Phenylpropyl 3-pyrrolidinopropyl ether 362665-82-5P 362665-85-8P 401805-28-5P, 1-[3-(4-Nitrophenoxy)propyl]-4-methylpiperidine 409127-50-0P, 2-Methyl-4-(3-piperidinopropylamino)quinoline 409127-54-4P, 7-Chloro-4-(4-piperidinobutylamino)quinoline 409127-57-7P, 4-(6-Piperidinohexylamino)quinoline 409127-58-8P, 2-Methyl-4-(6-piperidinohexylamino)quinoline 409127-62-4P, 7-Chloro-4-(8-piperidinooctylamino)quinoline 409127-63-5P, 7-Chloro-4-(10-piperidinodecylamino)quinoline 409127-84-0P, 10-Piperidinodecylamine 415936-57-1P, 1-[3-(4-Bromophenoxy)propyl]piperidine 462114-07-4P, 3,3-Dimethylbutyl 3-piperidinopropyl ether 462114-09-6P 462114-10-9P 462114-65-4P 462114-66-5P 462114-67-6P 462114-68-7P, 1-[3-(4-Cyanophenoxy)propyl]-4-methylpiperidine hydrochloride 462114-69-8P, 1-[3-(4-Cyanophenoxy)propyl]-3-methylpiperidine hydrochloride 462114-70-1P 462114-71-2P 462114-72-3P, 1-[3-[4-(3-Oxobutyl)phenoxy]propyl]piperidine hydrochloride 462114-73-4P, 1-[3-(4-Cyano-3-fluorophenoxy)propyl]piperidine hydrochloride 462114-74-5P, 1-[3-(4-Nitrophenoxy)propyl]-3-methylpiperidine 462114-75-6P, 1-[3-(4-Nitrophenoxy)propyl]-3-methylpiperidine hydrogen oxalate 462114-76-7P, 1-[3-(4-Cyanophenoxy)propyl]-2-methylpiperidine hydrochloride 462114-77-8P, 1-[3-(4-Nitrophenoxy)propyl]-2-methylpiperidine 462114-78-9P, 1-[3-(4-Nitrophenoxy)propyl]-2-methylpiperidine hydrogen oxalate 462114-79-0P 462114-80-3P 462114-81-4P 462114-82-5P, 1-[3-(4-Propionylphenoxy)propyl]-3-methylpiperidine hydrogen oxalate 462114-83-6P, 1-[3-[4-(Cyclobutylcarbonyl)phenoxy]propyl]piperidine 462114-84-7P 462114-85-8P, 1-[3-[4-(Cyclopentylcarbonyl)phenoxy]propyl]piperidine 462114-86-9P 462114-87-0P, 1-[3-(4-Cyanophenoxy)propyl]-cis-2-methyl-5-ethylpiperidine 462114-88-1P 462114-89-2P, 1-[3-(4-Cyanophenoxy)propyl]-trans-2-methyl-5-ethylpiperidine

462114-90-5P 462114-91-6P, 1-[3-(4-Cyanophenoxy)propyl]-cis-3,5-dimethylpiperidine 462114-92-7P, 1-[3-(4-Cyanophenoxy)propyl]-cis-3,5-dimethylpiperidine hydrogen oxalate 462114-93-8P 462114-94-9P 462114-95-0P 462114-96-1P, 1-[3-(4-Propionylphenoxy)propyl]-2-methylpiperidine hydrogen oxalate 462114-97-2P, 1-[3-[4-(1-Hydroxypropyl)phenoxy]propyl]-3-methylpiperidine 462114-98-3P, 1-[3-[4-(1-Hydroxypropyl)phenoxy]propyl]-3-methylpiperidine hydrogen oxalate 462114-99-4P, 1-[3-[4-(1-Hydroxypropyl)phenoxy]propyl]-4-methylpiperidine 462115-00-0P, 1-[3-[4-(1-Hydroxypropyl)phenoxy]propyl]-4-methylpiperidine hydrogen oxalate 462115-01-1P, 1-[3-(4-Propionylphenoxy)propyl]-2-methylpiperidine oxime hydrochloride 462115-03-3P, 1-[3-(4-Propionylphenoxy)propyl]-4-methylpiperidine methoxime hydrogen oxalate 462115-04-4P, 1-[3-(4-Cyanophenoxy)propyl]-trans-3,5-dimethylpiperidine 462115-05-5P, 1-[3-(4-Cyanophenoxy)propyl]trans-3,5-dimethylpiperidine hydrogen oxalate 462115-06-6P, 1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]-trans-3,5-dimethylpiperidine 462115-07-7P, 1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]-trans-3,5-dimethylpiperidine hydrogen oxalate 462115-08-8P, 1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]-cis-3,5-dimethylpiperidine 462115-09-9P 462115-10-2P, 1-[3-(4-Carbomethoxyphenoxy)propyl]piperidine 462115-11-3P, 1-[3-(4-Carbomethoxyphenoxy)propyl]piperidine hydrogen oxalate 462115-12-4P 462115-13-5P 462115-14-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(H3 receptor modulator; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT 462115-15-7P, 1-[3-[4-(1-Ethoxypropyl)phenoxy]propyl]-2-methylpiperidine 462115-16-8P 462115-17-9P 462115-18-0P, 1-[3-(4-Propionylphenoxy)propyl]-4-methylpiperidine oxime hydrogen oxalate 462115-19-1P, 1-[3-(4-Bromophenoxy)propyl]piperidine hydrogen oxalate 462115-20-4P, 1-[3-(4-Nitrophenoxy)propyl]piperidine hydrogen oxalate 462115-22-6P 462115-23-7P 462115-24-8P, 1-[3-(4-Isopropylphenoxy)propyl]piperidine hydrogen oxalate 462115-25-9P, 1-[3-(4-sec-Butylphenoxy)propyl]piperidine 462115-26-0P 462115-27-1P 462115-28-2P, 1-[3-(4-Propylphenoxy)propyl]piperidine hydrogen oxalate 462115-29-3P 462115-30-6P, 1-[3-(4-Ethylphenoxy)propyl]piperidine hydrogen oxalate 462115-37-3P 462115-39-5P, 2-Benzothiazolyl 3-piperidinopropyl ether 462115-40-8P 462115-42-0P, 3-Cyclopentyl-N-[3-(1-pyrrolidinyl)propyl]propanamide 462115-43-1P, 3-Cyclopentyl-N-[3-(1-pyrrolidinyl)propyl]propanamide hydrogen oxalate 462115-44-2P 462115-45-3P 462115-46-4P 462115-47-5P 462115-48-6P 462115-49-7P 462115-50-0P 462115-51-1P 462115-54-4P, 5-Nitro-2-(6-piperidinohexyl)pyridine hydrogen oxalate 462115-56-6P, 3-Nitro-2-(6-piperidinohexylamino)pyridine 462115-57-7P, 3-Nitro-2-(6-piperidinohexylamino)pyridine hydrogen oxalate 462115-59-9P, 2-(6-Piperidinohexylamino)pyrimidine 462115-60-2P, 2-(6-Piperidinohexylamino)pyrimidine hydrogen oxalate 462115-61-3P 462115-62-4P 462115-63-5P 462115-64-6P 462115-65-7P 462115-66-8P 462115-67-9P 462115-68-0P 462115-69-1P 462115-70-4P 462115-71-5P 462115-72-6P 462115-73-7P 462115-74-8P 462115-75-9P 462115-76-0P 462115-77-1P 462115-78-2P 462115-79-3P 462115-80-6P 462115-81-7P 462115-82-8P 462115-83-9P 462115-84-0P 462115-85-1P 462115-86-2P 462115-87-3P 462115-88-4P, 4-(6-Piperidinohexylamino)quinoline dioxalate 462115-89-5P, 2-Methyl-4-(3-piperidinopropylamino)quinoline dioxalate 462115-90-8P, 2-Methyl-4-(6-piperidinohexylamino)quinoline dioxalate 462115-91-9P, 7-Chloro-4-(3-piperidinopropylamino)quinoline dioxalate 462115-92-0P, 7-Chloro-4-(4-piperidinobutylamino)quinoline dioxalate 462115-93-1P, 7-Chloro-4-(8-piperidinooctylamino)quinoline dioxalate 462115-94-2P, 7-Chloro-4-(10-piperidinodecylamino)quinoline dioxalate

462115-95-3P, 7-Chloro-4-(12-piperidinododecylamino)quinoline
462115-96-4P, 7-Chloro-4-(12-piperidinododecylamino)quinoline dioxalate
462115-97-5P, 7-Chloro-4-[[4-(3-piperidinopropoxy)phenyl]amino]quinoline
462115-98-6P, 7-Chloro-4-[[4-(3-piperidinopropoxy)phenyl]amino]quinoline
dioxalate 462115-99-7P, 7-Chloro-4-[[2-[4-(3-
piperidinopropoxy)phenyl]ethyl]amino]quinoline 462116-00-3P,
7-Chloro-4-[[2-[4-(3-piperidinopropoxy)phenyl]ethyl]amino]quinoline
dioxalate 462116-01-4P 462116-02-5P 462116-03-6P,
5-Nitro-2-(5-piperidinopentylamino)pyridine 462116-04-7P,
5-Nitro-2-(5-piperidinopentylamino)pyridine hydrogen oxalate
462116-06-9P, 3-Nitro-2-(5-piperidinopentylamino)pyridine hydrogen oxalate
462116-07-0P, 5-Amino-2-(5-piperidinopentylamino)pyridine 462116-08-1P,
5-Amino-2-(5-piperidinopentylamino)pyridine dioxalate 462116-09-2P,
2-(6-Piperidinohexylamino)quinoline 462116-10-5P, 2-(6-
Piperidinohexylamino)quinoline dioxalate 462116-11-6P 462116-12-7P,
2-(6-Piperidinohexylamino)benzothiazole 462116-13-8P 462116-14-9P,
10-Piperidinodecylamine dioxalate 462116-15-0P, 1-[3-(4-
Cyanophenoxy)propyl]-4-methylpiperidine 462116-16-1P,
1-[3-(4-Cyanophenoxy)propyl]-3-methylpiperidine 462116-17-2P,
1-[3-[4-(3-Oxobutyl)phenoxy]propyl]piperidine 462116-18-3P,
1-[3-(4-Cyano-3-fluorophenoxy)propyl]piperidine 462116-19-4P,
1-[3-(4-Cyanophenoxy)propyl]-2-methylpiperidine 462116-20-7P,
1-[3-(4-Cyanophenoxy)propyl]-2,6-dimethylpiperidine 462116-21-8P
462116-22-9P 462116-23-0P, 2-[(2-Piperidinoethyl)amino]benzothiazole
462116-24-1P, 2-Nitro-5-(6-piperidinohexyl)pyridine 462116-25-2P,
N-Benzyl-N'-(3-piperidinopropyl)guanidine 462116-26-3P,
N-Cyclohexylmethyl-N'-(3-piperidinopropyl)guanidine 462116-27-4P
462116-28-5P 462116-29-6P 462116-30-9P, N-(4-Bromobenzyl)-N'-(4-
piperidinobutyl)sulfamide 462116-31-0P, 3-Chloro-N-(4-piperidinobutyl)-N-
methylbenzenesulfonamide 462116-32-1P 462116-33-2P,
cis-1-(6-Cyclohexyl-3-hexen-1-yl)piperidine 462116-34-3P,
trans-1-(6-Cyclohexyl-3-hexen-1-yl)piperidine 462116-35-4P,
1-[2-(5,5-Dimethyl-1-hexyn-1-yl)cyclopropyl]piperidine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(H3 receptor modulator; prepn. of aryloxyalkylamines as
histamine H3 receptor modulators)

IT 24827-37-0P 54758-33-7P, (4-Hydroxyphenyl)cyclopentyl ketone
55154-90-0P 184031-01-4P, (4-Hydroxyphenyl)cyclobutyl ketone
462115-32-8P 462115-33-9P 462115-34-0P 462115-35-1P 462115-36-2P
462115-52-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(intermediate; prepn. of aryloxyalkylamines as **histamine** H3
receptor modulators)

IT 51-67-2, Tyramine 70-70-2, 4-Propionylphenol 86-98-6,
4,7-Dichloroquinoline 98-59-9, p-Toluene **sulfonyl** chloride
99-93-4, 4'-Hydroxyacetophenone 103-71-9, Phenyl isocyanate, reactions
104-58-5, 3-(1-Piperidinyl)propanol 104-86-9, 4-Chlorobenzylamine
104-97-2, 3-Cyclopentylpropionyl chloride 108-91-8, Cyclohexylamine,
reactions 108-95-2, Phenol, reactions 109-64-8, 1,3-Dibromopropane
109-89-7, Diethylamine, reactions 110-89-4, Piperidine, reactions
123-30-8, 4-Hydroxyaniline 123-75-1, Pyrrolidine, reactions 140-53-4,
4-Chlorobenzyl cyanide 156-87-6, 3-Aminopropanol 504-63-2,
1,3-Propanediol 532-55-8, Benzoyl isothiocyanate 588-63-6,
3-Phenoxypropyl bromide 589-29-7, 1,4-Benzenedimethanol 611-35-8,
4-Chloroquinoline 612-62-4, 2-Chloroquinoline 615-20-3,
2-Chlorobenzothiazole 622-93-5 623-24-5 626-56-2, 3-Methylpiperidine
626-58-4, 4-Methylpiperidine 637-59-2, 3-Phenylpropyl bromide

765-38-8, 2-Methylpyrrolidine 772-31-6, Cyclopropyl 4-fluorophenyl ketone 1074-82-4, Potassium phthalimide 1122-82-3, Cyclohexyl isothiocyanate 1722-12-9, 2-Chloropyrimidine 2430-16-2, 6-Phenylhexanol 2508-29-4, 5-Aminopentanol 2528-61-2, n-Heptanoyl chloride 2855-08-5, 3,3-Dimethylbutyl chloride 3173-53-3, Cyclohexyl isocyanate 3344-70-5, 1,12-Dibromododecane 3694-45-9, 4-Chlorobenzylisothiocyanate 3954-13-0, Pentyl isocyanate 4048-33-3, 6-Aminohexanol 4101-68-2, 1,10-Dibromodecane 4295-06-1, 4-Chloro-2-methylquinoline 4524-93-0, Cyclopentylcarbonyl chloride 4548-45-2, 2-Chloro-5-nitropyridine 4549-32-0, 1,8-Dibromooctane 4897-50-1, 1,4'-Bipiperidine 5006-22-4, Cyclobutylcarbonyl chloride 5470-18-8, 2-Chloro-3-nitropyridine 5471-51-2, 4-(4-Hydroxyphenyl)-2-butanone 5472-49-1, N-(3-Chloropropyl)piperidine hydrochloride 6280-87-1, 5-Chlorovaleronitrile 13325-10-5, 4-Aminobutanol 22809-37-6, 6-Bromohexanoyl chloride 22921-72-8, 1-Bromo-5-phenoxypentane 23159-07-1, 1-(3-Aminopropyl)pyrrolidine 23573-93-5 27578-60-5, 1-Piperidineethanamine 35794-11-7, 3,5-Dimethylpiperidine 41903-50-8, Hydroxyacetophenone 61270-21-1, 4'-(5-Bromopentoxy)phenyl methyl ketone 61440-60-6, 3-(4-Chlorophenyl)propyl mesylate 65623-98-5, 4'-(3-Bromopropoxy)acetophenone 68453-37-2, 4-(Piperidinomethyl)benzoic acid methyl ester 69804-99-5, 3-Phenylpropylmesylate 93381-28-3, 3-Bromo-2-(R)-methyl-1-propanol 98244-48-5, 3-Bromo-2-(S)-methyl-1-propanol 134994-15-3, 1-Bromo-5-(4-benzoylphenoxy)pentane 362666-04-4, 3-Piperidinopropanol hydrochloride 462115-31-7, 4'-(5-Bromopentoxy)phenyl benzyl ketone 462115-38-4 462115-41-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

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AN 2002:736933 CAPLUS
DN 137:247603
TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity
IN Bennani, Youssef L.; Faghih, Ramin; Dwight, Wesley J.; Vasudevan, Anil; Conner, Scott E.
PA USA
SO U.S. Pat. Appl. Publ., 62 pp., Cont.-in-part of U.S. Ser. No. 902,925.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002137931	A1	20020926	US 2002-44471	20020111
	US 2002035103	A1	20020321	US 2001-902925	20010711
	US 6515013	B2	20030204		
PRAI	US 2000-218084P	P	20000713		
	US 2001-902925	A2	20010711		

OS MARPAT 137:247603
TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity
AB Title compds. I [wherein Z = a bond or CH2; R1 = OR2, NR3R4, or 3-R5-4-R6-2,5-dioxoimidazolidinyl; R2 = H, alkoxycarbonyl, alkyl(carbonyl), aminocarbonyl, sulfono, or phosphono; R3 and R4 =

independently H, alkenyl(sulfonyl), alkenyl(oxy)carbonyl, alkoxycarbonyl, alkyl(sulfonyl), alkylcarbonyl, aminocarbonyl, aminosulfonyl, alkynyl(sulfonyl), alkynyl(oxy)carbonyl, (un)substituted (hetero)arylalkyl, or (hetero)arylalkenylcarbonyl, etc.; R5, R6, and R7 = independently H or alkyl; or R1 and R7 together form =O; R8 = (cyclo)alkylcarbonyl, (un)substituted aryl(carbonyl), arylcarbonylaryl, arylcarbonylheterocyclyl, cycloalkylcarbonylaryl, cycloalkylcarbonylheterocyclyl, heterocyclyl(carbonyl), heterocyclylcarbonylaryl, or heterocyclylcarbonylheterocyclyl; R9 = H or alkyl; RA, RB, RC, and RD = independently H, alkenyl, alkoxy(alkoxy), (alkoxy)alkyl, alkoxycarbonyl, alkylcarbonyl(oxy), alkylsulfinyl, alkylsulfonyl, alkylthio, alkynyl, amino(alkyl), aminocarbonyl, (carboxy)alkyl, (cyano)alkyl, formyl, halo(alkoxy), haloalkyl, (hydroxy)alkyl, SH, or NO2, etc.; and pharmaceutically acceptable salts] were prepd. as **histamine**-3 receptor ligands. For example, 4'-[3-[(3R)-3-aminopyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile in CH2Cl2 was treated with polymer supported N,N-diisopropylethylamine, catalytic amt. of DMAP, and 4-methoxybenzenesulfonyl chloride. After shaking at ambient temp. for 14 h, the mixt. was treated with tris(2-aminoethyl)amine-polystyrene resin and the mixt. shaken for an addnl. 2 h to give the [[(biphenylyloxy)propyl]pyrrolidinyl]benzenesulfonamide II (79%). The latter bound to the **histamine**-3 receptor with Ki of 12 nM. I are useful for the treatment of acute myocardial infarction, asthma, bipolar disorder, cognitive enhancement, cutaneous carcinoma, depression, gastrointestinal disorders, inflammation, jet lag, medullary thyroid carcinoma, melanoma, Meniere's disease, migraine, motion sickness, obesity, pain, Parkinson's disease, schizophrenia, seizures, septic shock, Tourette's syndrome, Vertigo, wakefulness, **Alzheimer**'s disease, attention-deficit hyperactivity disorder (ADHD), epilepsy, and narcolepsy (no data).

ST aryloxypropylpyrrolidine prepn **histamine** receptor ligand; biphenylyloxypropylpyrrolidine prepn **Alzheimers** disease ADHD epilepsy obesity narcolepsy treatment

IT Sleep
(-waking cycle; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Brain, disease
(Gilles de la Tourette syndrome; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT **Histamine** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H3; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Ear
(Meniere's disease, treatment; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Mental disorder
(attention deficit hyperactivity disorder, treatment; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Rhythm, biological
(circadian, jet lag; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of

Alzheimer's disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Mental disorder
(cognitive, psychiatric disorder; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Mental disorder
(depression; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Digestive tract
(disease; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Cognition
(disorder, psychiatric disorder; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Heart, disease
(infarction; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Mental disorder
(manic bipolar disorder; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Thyroid gland, neoplasm
(medullary carcinoma, treatment; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Headache
(migraine; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Sleep
(narcolepsy, treatment; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT **Alzheimer**'s disease
Analgesics
Anti-**Alzheimer**'s agents
Anti-inflammatory agents
Antiasthmatics
Anticonvulsants
Antidepressants
Antimigraine agents
Antiobesity agents
Antiparkinsonian agents
Asthma
Carcinoma
Cardiovascular agents
Cognition enhancers
Dizziness
Epilepsy
Human
Inflammation
Melanoma
Obesity

Parkinson's disease
Seizures
(prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Shock (circulatory collapse)
(septic, treatment; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Motion sickness
Schizophrenia
(treatment; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT 392337-21-2P, 4'-[3-((3R)-3-Aminopyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-14-6P 392338-16-8P 392338-59-9P 392338-60-2P, 4'-[3-(3-Oxo-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**histamine**-3 receptor ligand; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT 392337-05-2P 392337-07-4P 392337-08-5P 392337-09-6P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-2-(3-pyridinyl)-1,3-thiazole-4-carboxamide 392337-10-9P 392337-11-0P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-2-propanesulfonamide 392337-12-1P 392337-13-2P 392337-14-3P, (5S)-3-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-5-methyl-2,4-imidazolidinedione 392337-15-4P 392337-16-5P, 4-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-17-6P 392337-18-7P 392337-19-8P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-4-cyanobenzamide 392337-20-1P 392337-22-3P 392337-23-4P 392337-24-5P 392337-25-6P 392337-26-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-methoxybenzenesulfonamide 392337-27-8P 392337-28-9P 392337-29-0P 392337-30-3P 392337-31-4P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-methylbenzenesulfonamide 392337-32-5P, 3-Chloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluorobenzenesulfonamide 392337-33-6P 392337-34-7P 392337-35-8P 392337-36-9P 392337-37-0P, 3-Chloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-38-1P 392337-39-2P 392337-40-5P 392337-41-6P 392337-42-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-thiophenesulfonamide 392337-43-8P 392337-44-9P 392337-45-0P 392337-46-1P 392337-47-2P, 4-Butoxy-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-48-3P 392337-49-4P 392337-50-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-phenylethenesulfonamide 392337-51-8P 392337-52-9P 392337-53-0P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-3-methylbenzenesulfonamide 392337-54-1P 392337-55-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2,4-difluorobenzenesulfonamide 392337-56-3P 392337-57-4P 392337-58-5P, 3,4-Dichloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-59-6P 392337-60-9P, 4-Bromo-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-61-0P 392337-62-1P 392337-63-2P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolid

inyl]-4-methoxybenzenesulfonamide 392337-64-3P, 4-tert-Butyl-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-65-4P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-methylbenzenesulfonamide 392337-66-5P 392337-67-6P 392337-68-7P 392337-69-8P, 3-Chloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-fluorobenzenesulfonamide 392337-70-1P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-ethylbenzenesulfonamide 392337-71-2P 392337-72-3P 392337-73-4P 392337-74-5P, 3-Chloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-75-6P, 3-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-76-7P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-3-fluorobenzenesulfonamide 392337-77-8P 392337-78-9P 392337-79-0P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-5-isoquinolinesulfonamide 392337-80-3P 392337-81-4P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-3,4-dichlorobenzenesulfonamide 392337-82-5P 392337-84-7P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-4-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]oxy]benzenesulfonamide 392337-85-8P 392337-86-9P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-2-thiophenesulfonamide 392337-87-0P 392337-88-1P 392337-89-2P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-8-quinolinesulfonamide 392337-90-5P 392337-92-7P 392337-93-8P 392337-94-9P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-2-phenylethenesulfonamide 392337-95-0P 392337-96-1P, 2-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-97-2P 392337-98-3P 392337-99-4P 392338-00-0P 392338-01-1P 392338-02-2P, 3,4-Dichloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392338-03-3P 392338-04-4P 392338-05-5P 392338-06-6P 392338-08-8P 392338-09-9P 392338-10-2P 392338-11-3P 392338-12-4P, N-[2-Chloro-4-[[[(3R)-1-[3-[4-(2-pyridinyl)phenoxy]propyl]pyrrolidinyl]amino]**sulfonyl**]phenyl]acetamide 392338-13-5P, 4'-[3-[(3R)-3-(Dimethylamino)pyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile 392338-17-9P 392338-18-0P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,3,3-trimethylbutanamide 392338-19-1P 392338-20-4P 392338-21-5P 392338-22-6P 392338-23-7P, N'-tert-Butyl-N-[(3R)-1-[3-[[4'-cyano(,1'-biphenyl)-4-yl]oxy]propyl]pyrrolidinyl]-N-methylurea 392338-24-8P 392338-25-9P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluoro-N-methylbenzamide 392338-26-0P 392338-27-1P 392338-28-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-methyl-2-furamide 392338-29-3P 392338-30-6P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,N',N'-trimethylsulfamide 392338-31-7P 392338-32-8P 392338-33-9P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-isopropyl-N-methylbenzenesulfonamide 392338-34-0P 392338-35-1P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluoro-N-(4-fluorobenzoyl)benzamide 392338-36-2P 392338-37-3P 392338-38-4P, Allyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-39-5P, Methyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-40-8P, tert-Pentyl (3R)-1-[3-[(4'-cyano [1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-41-9P 392338-42-0P 392338-43-1P 392338-44-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-morpholinecarboxamide 392338-45-3P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluorobenzamide 392338-46-4P 392338-47-5P 392338-48-6P 392338-49-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-

yl)oxy]propyl]pyrrolidinyl]-2-(3-pyridinyl)-1,3-thiazole-4-carboxamide 392338-50-0P 392338-51-1P, N'-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,N-dimethylsulfamide 392338-52-2P 392338-53-3P 392338-54-4P 392338-55-5P 392338-56-6P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-(4-morpholinylcarbonyl)-4-morpholinecarboxamide 392338-57-7P, Cyclopropyl[4-[3-(3-hydroxy-1-pyrrolidinyl)propoxy]phenyl]methanone 392338-58-8P 392338-61-3P 392338-62-4P, 4'-[3-(3-Hydroxy-3-methyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-63-5P, 4'-[3-(3-Hydroxy-3-isopropyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-64-6P 392338-66-8P 392338-67-9P, N,N-Dimethyl-N-[(3S)-1-[3-[[4'-(1-pyrrolidinylcarbonyl)[1,1'-biphenyl]-4-yl]oxy]propyl]pyrrolidinyl]amine 392338-68-0P 392338-69-1P 392338-71-5P 392338-72-6P, N-[(3R)-1-[3-[[4'-Cyano(,1'-biphenyl)-4-yl]oxy]propyl]pyrrolidinyl]-3-fluorobenzenesulfonamide 392338-73-7P 461045-01-2P 461045-03-4P 461045-05-6P 461045-07-8P 461045-10-3P 461045-12-5P 461045-14-7P 461045-17-0P 461045-20-5P 461045-24-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**histamine**-3 receptor ligand; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT 36116-18-4P, Cyclopropyl(4-hydroxyphenyl)methanone 104582-67-4P 104582-73-2P 123843-58-3P 123864-93-7P, 3-Fluoro-4'-methoxy-1,1'-biphenyl-4-carbonitrile 133057-85-9P 149505-48-6P 149506-22-9P 360553-46-4P, [4-(3-Chloropropoxy)phenyl](cyclopropyl)methanone 392337-06-3P, 1-[4-[3-((3R)-3-Aminopyrrolidinyl)propoxy]phenyl]ethanone 392338-07-7P, (3R)-1-[3-[4-(2-Pyridinyl)phenoxy]propyl]pyrrolidinylamine 460746-47-8P 460748-04-3P 460748-08-7P 461045-02-3P 461045-04-5P 461045-06-7P 461045-08-9P 461045-09-0P 461045-11-4P 461045-13-6P 461045-15-8P 461045-16-9P 461045-18-1P 461045-19-2P 461045-21-6P 461045-23-8P 461045-25-0P 461045-26-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

IT 59-67-6, Nicotinic acid, reactions 70-70-2, 1-(4-Hydroxyphenyl)-1-propanone 79-44-7, Dimethylcarbamyl chloride 98-09-9, Benzenesulfonyl chloride 98-68-0, 4-Methoxybenzenesulfonyl chloride 99-93-4, 1-(4-Hydroxyphenyl)ethanone 109-70-6, 1-Bromo-3-chloropropane 133-59-5, 2-Methylbenzenesulfonyl chloride 403-43-0, 4-Fluorobenzoyl chloride 527-69-5, 2-Furoyl chloride 619-65-8, 4-Cyanobenzoic acid 701-27-9, 3-Fluorobenzenesulfonyl chloride 1068-55-9, Isopropylmagnesium chloride 1138-56-3, 4-Butoxybenzenesulfonyl chloride 1192-63-8, 1-Pyrrolidinecarbonyl chloride 1759-53-1, Cyclopropanecarboxylic acid 2105-94-4, 4-Bromo-2-fluorophenol 2362-12-1, 4-Bromo-2-methylphenol 2799-21-5 2937-50-0, Allyl chloroformate 3794-80-7, 1,1-Dimethylpropyl chloroformate 3964-56-5, 4-Bromo-2-chlorophenol 5720-07-0, 4-Methoxyphenylboronic acid 6068-72-0, 4-Cyanobenzoyl chloride 7065-46-5, tert-Butylacetyl chloride 7150-55-2 7368-78-7, 4-Bromo-2-methoxyphenol 7764-95-6, (2R)-2-[(tert-Butoxycarbonyl)amino]propanoic acid 10147-37-2, 2-Propanesulfonyl chloride 10400-19-8, Nicotinoyl chloride 13360-57-1, Dimethylsulfamoyl chloride 14472-14-1, 4-Bromo-3-methylphenol 15159-40-7, 4-Morpholinecarbonyl chloride 15761-38-3, (2S)-2-[(tert-Butoxycarbonyl)amino]propanoic acid 19812-93-2, 4'-Hydroxy[1,1'-biphenyl]-4-carbonitrile 39067-29-3, 2-(3-Pyridinyl)-1,3-thiazole-4-

carboxylic acid 40499-83-0, 3-Hydroxypyrrolidine 41891-21-8, tert-Butylcarbamoyl chloride 41963-20-6, 4-Bromo-3-methylbenzonitrile 46118-95-0, [(4-Methyl-2-pyrimidinyl)sulfanyl]acetic acid 49584-26-1, 4-Cyanobenzenesulfonyl chloride 51035-40-6, 4-(2-Pyridinyl)phenol 56542-67-7, 3-Cyanobenzenesulfonyl chloride 67832-11-5, 4-Bromo-2-methylbenzonitrile 68835-89-2, Di(tert-pentyl) dicarbonate 71530-58-0 82964-91-8, 4-(Methylsulfonyl)benzenesulfonyl chloride 94108-56-2, 4-(Trifluoromethoxy)benzenesulfonyl chloride 100243-39-8, (3S)-3-Pyrrolidinol 104197-13-9, 4-Bromo-2,6-difluorophenol 105942-08-3, 4-Bromo-2-fluorobenzonitrile 122536-77-0 126747-14-6, 4-Cyanophenylboronic acid 132883-44-4, N,N-Dimethyl-N-((3S)-pyrrolidinyl)amine 132958-72-6, N,N-Dimethyl-N-((3R)-pyrrolidinyl)amine 161045-79-0 180992-31-8, 2-(3-Pyridinyl)-1,3-thiazole-4-carbonyl chloride 372514-08-4, 1-[[4'-(3-Chloropropoxy)[1,1'-biphenyl]-4-yl]carbonyl]pyrrolidine 392337-91-6, [4-[3-((3R)-3-Aminopyrrolidinyl)propoxy]phenyl](cyclopropyl)methanone 392338-15-7 392338-65-7, (3R)-3-Methyl-3-pyrrolidinol 392338-70-4, 1-[4-(3-Chloropropoxy)phenyl]-4-(1-pyrrolidinylcarbonyl)piperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, narcolepsy, and obesity)

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS

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DN 136:263087
TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy
IN Bennani, Youssef L.; Faghih, Ramin; Dwight, Wesley J.; Vasudevan, Anil; Conner, Scott E.
PA USA
SO U.S. Pat. Appl. Publ., 54 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002035103	A1	20020321	US 2001-902925	20010711
	US 6515013	B2	20030204		
	US 2002137931	A1	20020926	US 2002-44471	20020111
PRAI	US 2000-218084P	P	20000713		
	US 2001-902925	A2	20010711		

OS MARPAT 136:263087
TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy
AB Title compds. I [wherein Z = a bond or CH2; R1 = OR2, NR3R4, or substituted 2,5-dioxoimidazolidinyl; R2 = H, alkoxycarbonyl, alkyl(carbonyl), aminocarbonyl, sulfono, or phosphono; R3 and R4 = independently H, alkenyl(sulfonyl), alkenyl(oxy)carbonyl, alkoxycarbonyl, alkyl(sulfonyl), alkylcarbonyl, aminocarbonyl, aminosulfonyl, alkynyl(sulfonyl), alkynyl(oxy)carbonyl, or (un)substituted (hetero)arylalkyl, (hetero)arylalkenylcarbonyl, etc.; R7 = H or alkyl; or R1 and R7 together form :O; R8 = (cyclo)alkylcarbonyl, or (un)substituted aryl(carbonyl), arylcarbonylaryl, arylcarbonylheterocyclyl, cycloalkylcarbonylaryl, cycloalkylcarbonylheterocyclyl,

heterocyclyl(carbonyl), heterocyclylcarbonylaryl, or heterocyclylcarbonylheterocyclyl; R9 = H or alkyl] were prepd. as **histamine**-3 receptor ligands. For example, 4'-[3-[(3R)-3-aminopyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile in CH2Cl2 was treated with polymer supported N,N-diisopropylethylamine, catalytic N,N-dimethylaminopyridine, and 4-methoxybenzenesulfonyl chloride. After shaking at ambient temp. for 14 h, the mixt. was treated with tris(2-aminoethyl)amine-polystyrene resin and the mixt. shaken for an addnl. 2 h to give the [[(biphenylyloxy)propyl]pyrrolidinyl]benzenesulfonamide II (79%). The latter bound to the **histamine**-3 receptor with Ki of 12 nM. I are useful for the treatment of acute myocardial infarction, asthma, cutaneous carcinoma, depression, inflammation, medullary thyroid carcinoma, melanoma, Meniere's disease, migraine, motion sickness, obesity, pain, Parkinson's disease, schizophrenia, seizures, septic shock, **Alzheimer**'s disease, attention-deficit hyperactivity disorder (ADHD), epilepsy, and narcolepsy.

ST aryloxypropyl pyrrolidine prepn **histamine** receptor ligand; biphenylyloxypropyl pyrrolidine prepn **Alzheimers** disease ADHD epilepsy narcolepsy treatment

IT **Histamine** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H3; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT Ear
(Meniere's disease, treatment; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT Mental disorder
(attention deficit hyperactivity disorder, treatment; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT Antitumor agents
(carcinoma; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT Heart, disease
(infarction, therapeutic agents; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT Thyroid gland, neoplasm
(medullary carcinoma, treatment; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT Antitumor agents
(melanoma; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT Sleep
(narcolepsy, treatment; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT Analgesics
Anti-**Alzheimer**'s agents
Anti-inflammatory agents
Antiasthmatics
Anticonvulsants
Antidepressants
Antimigraine agents

Antiobesity agents
Antiparkinsonian agents
Human
(prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT Shock (circulatory collapse)
(septic, treatment; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT Motion sickness
Schizophrenia
(treatment; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT 392337-21-2P, 4'-[3-((3R)-3-Aminopyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-14-6P 392338-16-8P 392338-59-9P 392338-60-2P, 4'-[3-(3-Oxo-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**histamine**-3 receptor ligand; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT 392337-05-2P 392337-07-4P 392337-08-5P 392337-09-6P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-2-(3-pyridinyl)-1,3-thiazole-4-carboxamide 392337-10-9P 392337-11-0P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-2-propanesulfonamide 392337-12-1P 392337-13-2P 392337-14-3P, (5S)-3-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-5-methyl-2,4-imidazolidinedione 392337-15-4P 392337-16-5P, 4-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-17-6P 392337-18-7P 392337-19-8P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-4-cyanobenzamide 392337-20-1P 392337-22-3P 392337-23-4P 392337-24-5P 392337-25-6P 392337-26-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-methoxybenzenesulfonamide 392337-27-8P 392337-28-9P 392337-29-0P 392337-30-3P 392337-31-4P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-methylbenzenesulfonamide 392337-32-5P, 3-Chloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluorobenzenesulfonamide 392337-33-6P 392337-34-7P 392337-35-8P 392337-36-9P 392337-37-0P, 3-Chloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-38-1P 392337-39-2P 392337-40-5P 392337-41-6P 392337-42-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-thiophenesulfonamide 392337-43-8P 392337-44-9P 392337-45-0P 392337-46-1P 392337-47-2P, 4-Butoxy-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-48-3P 392337-49-4P 392337-50-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-phenylethenesulfonamide 392337-51-8P 392337-52-9P 392337-53-0P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-3-methylbenzenesulfonamide 392337-54-1P 392337-55-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2,4-difluorobenzenesulfonamide 392337-56-3P 392337-57-4P 392337-58-5P, 3,4-Dichloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-59-6P 392337-60-9P, 4-Bromo-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-61-0P 392337-62-1P

392337-63-2P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-methoxybenzenesulfonamide 392337-64-3P, 4-tert-Butyl-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-65-4P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-methylbenzenesulfonamide 392337-66-5P 392337-67-6P 392337-68-7P 392337-69-8P, 3-Chloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-fluorobenzenesulfonamide 392337-70-1P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-ethylbenzenesulfonamide 392337-71-2P 392337-72-3P 392337-73-4P 392337-74-5P, 3-Chloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-75-6P, 3-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-76-7P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-3-fluorobenzenesulfonamide 392337-77-8P 392337-78-9P 392337-79-0P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-5-isoquinolinesulfonamide 392337-80-3P 392337-81-4P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-3,4-dichlorobenzenesulfonamide 392337-82-5P 392337-84-7P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-4-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]oxy]benzenesulfonamide 392337-85-8P 392337-86-9P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-2-thiophenesulfonamide 392337-87-0P 392337-88-1P 392337-89-2P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-8-quinolinesulfonamide 392337-90-5P 392337-92-7P 392337-93-8P 392337-94-9P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-2-phenylethenesulfonamide 392337-95-0P 392337-96-1P, 2-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-97-2P 392337-98-3P 392337-99-4P 392338-00-0P 392338-01-1P 392338-02-2P, 3,4-Dichloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392338-03-3P 392338-04-4P 392338-05-5P 392338-06-6P 392338-08-8P 392338-09-9P 392338-10-2P 392338-11-3P 392338-12-4P, N-[2-Chloro-4-[[[(3R)-1-[3-[4-(2-pyridinyl)phenoxy]propyl]pyrrolidinyl]amino]**sulfonyl**]phenyl]acetamide 392338-13-5P, 4'-[3-[(3R)-3-(Dimethylamino)pyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile 392338-17-9P 392338-18-0P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,3,3-trimethylbutanamide 392338-19-1P 392338-20-4P 392338-21-5P 392338-22-6P 392338-23-7P, N'-tert-Butyl-N-[(3R)-1-[3-[[4'-cyano(,1'-biphenyl)-4-yl]oxy]propyl]pyrrolidinyl]-N-methylurea 392338-24-8P 392338-25-9P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluoro-N-methylbenzamide 392338-26-0P 392338-27-1P 392338-28-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-methyl-2-furamide 392338-29-3P 392338-30-6P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,N',N'-trimethylsulfamide 392338-31-7P 392338-32-8P 392338-33-9P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-isopropyl-N-methylbenzenesulfonamide 392338-34-0P 392338-35-1P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluoro-N-(4-fluorobenzoyl)benzamide 392338-36-2P 392338-37-3P 392338-38-4P, Allyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-39-5P, Methyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-40-8P, tert-Pentyl (3R)-1-[3-[(4'-cyano [1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-41-9P 392338-42-0P 392338-43-1P 392338-44-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-morpholinecarboxamide 392338-45-3P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluorobenzamide 392338-46-4P 392338-47-5P 392338-48-6P

392338-49-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-(3-pyridinyl)-1,3-thiazole-4-carboxamide 392338-50-0P 392338-51-1P, N'-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,N-dimethylsulfamide 392338-52-2P 392338-53-3P 392338-54-4P 392338-55-5P 392338-56-6P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-(4-morpholinylcarbonyl)-4-morpholinecarboxamide 392338-57-7P 392338-58-8P, Cyclopropyl[4-[3-((3R)-3-hydroxypyrrolidinyl)propoxy]phenyl]methanone 392338-61-3P, 4'-[3-((3S)-3-Hydroxypyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-62-4P, 4'-[3-(3-Hydroxy-3-methyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-63-5P, 4'-[3-(3-Hydroxy-3-isopropyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-64-6P, 4'-[3-((3R)-3-Hydroxy-3-methylpyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-66-8P 392338-67-9P, N,N-Dimethyl-N-[(3S)-1-[3-[[4'-(1-pyrrolidinylcarbonyl)[1,1'-biphenyl]-4-yl]oxy]propyl]pyrrolidinyl]amine 392338-68-0P 392338-69-1P 392338-71-5P 392338-72-6P, N-[(3R)-1-[3-[[4'-Cyano(,1'-biphenyl)-4-yl]oxy]propyl]pyrrolidinyl]-3-fluorobenzenesulfonamide 392338-73-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**histamine**-3 receptor ligand; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT 36116-18-4P, Cyclopropyl(4-hydroxyphenyl)methanone 360553-46-4P, [4-(3-Chloropropoxy)phenyl](cyclopropyl)methanone 392337-06-3P, 1-[4-[3-[(3R)-3-Aminopyrrolidinyl]propoxy]phenyl]ethanone 392338-07-7P, (3R)-1-[3-[4-(2-Pyridinyl)phenoxy]propyl]pyrrolidinylamine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer**'s disease, ADHD, epilepsy, and narcolepsy)

IT 59-67-6, Nicotinic acid, reactions 70-70-2, 1-(4-Hydroxyphenyl)-1-propanone 79-44-7, Dimethylcarbamyl chloride 98-09-9, Benzenesulfonyl chloride 98-68-0, 4-Methoxybenzenesulfonyl chloride 99-93-4, 1-(4-Hydroxyphenyl)ethanone 109-70-6, 1-Bromo-3-chloropropane 133-59-5, 2-Methylbenzenesulfonyl chloride 403-43-0, 4-Fluorobenzoyl chloride 527-69-5, 2-Furoyl chloride 619-65-8, 4-Cyanobenzoic acid 701-27-9, 3-Fluorobenzenesulfonyl chloride 1068-55-9, Isopropylmagnesium chloride 1138-56-3, 4-Butoxybenzenesulfonyl chloride 1192-63-8, 1-Pyrrolidinecarbonyl chloride 1759-53-1, Cyclopropanecarboxylic acid 2799-21-5, 3-(3R)-Hydroxypyrrolidine 2937-50-0, Allyl chloroformate 3794-80-7, 1,1-Dimethylpropyl chloroformate 6068-72-0, 4-Cyanobenzoyl chloride 7065-46-5, tert-Butylacetyl chloride 7150-55-2 7764-95-6, (2R)-2-[(tert-Butoxycarbonyl)amino]propanoic acid 10147-37-2, 2-Propanesulfonyl chloride 10400-19-8, Nicotinoyl chloride 13360-57-1, Dimethylsulfamoyl chloride 15159-40-7, 4-Morpholinecarbonyl chloride 15761-38-3, (2S)-2-[(tert-Butoxycarbonyl)amino]propanoic acid 19812-93-2, 4'-Hydroxy[1,1'-biphenyl]-4-carbonitrile 39067-29-3, 2-(3-Pyridinyl)-1,3-thiazole-4-carboxylic acid 40499-83-0, 3-Hydroxypyrrolidine 41891-21-8, tert-Butylcarbamoyl chloride 46118-95-0, [(4-Methyl-2-pyrimidinyl)sulfanyl]acetic acid 49584-26-1, 4-Cyanobenzenesulfonyl chloride 51035-40-6, 4-(2-Pyridinyl)phenol 56542-67-7, 3-Cyanobenzenesulfonyl chloride 68835-89-2, Di(tert-pentyl) dicarbonate 71530-58-0 82964-91-8, 4-(Methylsulfonyl)benzenesulfonyl chloride 94108-56-2, 4-(Trifluoromethoxy)benzenesulfonyl chloride 100243-39-8, (3S)-3-Pyrrolidinol 122536-77-0 132883-44-4, N,N-Dimethyl-N-((3S)-pyrrolidinyl)amine 132958-72-6,

N,N-Dimethyl-N-((3R)-pyrrolidinyl)amine 180992-31-8,
2-(3-Pyridinyl)-1,3-thiazole-4-carbonyl chloride 372514-08-4,
1-[[4'-(3-Chloropropoxy)[1,1'-biphenyl]-4-yl]carbonyl]pyrrolidine
392337-91-6, [4-[3-((3R)-3-Aminopyrrolidinyl)propoxy]phenyl](cyclopropyl)m
ethanone 392338-15-7 392338-65-7, (3R)-3-Methyl-3-pyrrolidinol
392338-70-4, 1-[4-(3-Chloropropoxy)phenyl]-4-(1-
pyrrolidinylcarbonyl)piperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of di- and trisubstituted pyrrolidines as
histamine-3 receptor ligands for treatment of **Alzheimer**
's disease, ADHD, epilepsy, and narcolepsy)

=> **d his**

(FILE 'HOME' ENTERED AT 06:05:56 ON 20 JUN 2003)

FILE 'CAPLUS' ENTERED AT 06:06:21 ON 20 JUN 2003
E DEMENTIA/CT

FILE 'CAPLUS, WPIDS, MEDLINE, EMBASE' ENTERED AT 06:07:28 ON 20 JUN 2003
L1 172320 S DEMENTIA OR ALZHEIMER?
L2 182615 S L1 OR NEURODEGENERAT? DISEASE#
L3 1127914 S ((SULFONYLAMIDO OR SULFONYL AMIDO) (2A) HISTAMINE) OR NSAID O
L4 3550 S L2 (L) L3
L5 0 S L4 AND ((SULFONYLAMIDO (5A) HISTAMINE) OR (SULFONYL (5A) AMI
L6 24 S L4 AND HISTAMINE
L7 496 S L2 AND HISTAMINE
L8 3 S L7 AND (HISTAMINE (10A) SULFONYL)

=> **file reg**

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DICTIONARY FILE UPDATES: 18 JUN 2003 HIGHEST RN 533863-98-8

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Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STNote 27, Searching Properties
in the CAS Registry File, for complete details:

http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

```
=> s histamine and (sulfonyl (3a) amido)
           484 HISTAMINE
        862550 SULFONYL
         89443 AMIDO
          2885 SULFONYL (3A) AMIDO
L9           0 HISTAMINE AND (SULFONYL (3A) AMIDO)

=> s histamine and sulfonyl
           484 HISTAMINE
        862550 SULFONYL
L10          0 HISTAMINE AND SULFONYL

=> s histamine and sulfon?
           484 HISTAMINE
       1441970 SULFON?
L11          0 HISTAMINE AND SULFON?

=> s histamine and sulfo?
           484 HISTAMINE
       1539676 SULFO?
L12          0 HISTAMINE AND SULFO?

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                                                      ENTRY    SESSION
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FILE COVERS 1907 - 20 Jun 2003  VOL 138 ISS 26
FILE LAST UPDATED: 19 Jun 2003  (20030619/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s sulfonylamido (5a) histamine/ab
            57 SULFONYLAMIDO
         49170 HISTAMINE/AB
L13          1 SULFONYLAMIDO (5A) HISTAMINE/AB
```

=> d hit

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

Citing References

AB **Sulfonylamido**(ureido) derivs. of **histamine** were synthesized by an original procedure in order to obtain tight-binding activators of the zinc enzyme carbonic anhydrase (CA), exploiting the binding energy of the alkyl/arylsulfonyl moieties with amino acid residues at the entrance of the active site. In contrast to the lead mol., histamine, the new derivs. possessed higher affinity for three different CA isoenzymes, as evidenced by comparing the affinity consts. of these compds. for isoenzyme CA II.

=> d bib

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

Full Text | Citing References

AN 1999:504279 CAPLUS
DN 131:286325
TI Novel carbonic anhydrase isozymes I, II and IV activators incorporating sulfonyl-histamino moieties
AU Briganti, Fabrizio; Scozzafava, Andrea; Supuran, Claudiu T.
CS Universita degli Studi, Laboratorio di Chimica Inorganica e Bioinorganica, Florence, 50121, Italy
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(14), 2043-2048
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

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AN 1999:504279 CAPLUS
DN 131:286325
TI Novel carbonic anhydrase isozymes I, II and IV activators incorporating sulfonyl-histamino moieties
AU Briganti, Fabrizio; Scozzafava, Andrea; Supuran, Claudiu T.
CS Universita degli Studi, Laboratorio di Chimica Inorganica e Bioinorganica, Florence, 50121, Italy
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(14), 2043-2048
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB **Sulfonylamido**(ureido) derivs. of **histamine** were synthesized by an original procedure in order to obtain tight-binding activators of the zinc enzyme carbonic anhydrase (CA), exploiting the binding energy of the alkyl/arylsulfonyl moieties with amino acid residues at the entrance of the active site. In contrast to the lead mol., histamine, the new derivs. possessed higher affinity for three different CA isoenzymes, as evidenced by comparing the affinity consts. of these compds. for isoenzyme CA II.

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AN 2000:575630 CAPLUS
DN 133:129891
TI Medicine for treating senility dementia, parkinsonism and cardiocerebral angiopathy
IN Lu, Gao
PA Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 14 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1228995	A	19990922	CN 1999-113434	19990126
PRAI	CN 1999-113434		19990126		

AB One or more of nerve growth factor, brain-derived neurotrophic factor, nerve trophic factor-3, nerve trophic factor-4, nerve trophic factor-5, ciliary neurotropic factor, fibroblast growth factor, epidermal growth factor, ganglioside, acetylcholine, histamine, calcitonin gene-related peptide, neuropeptide, cAMP, atrial natriuretic peptide, brain natriuretic peptide, C-type natriuretic peptide, PGI2, and EDRF are used for treatment of senility dementia, parkinsonism, cardiocerebral angiopathy, coronary heart disease, hypertension, and atheromatosis.

AN 1997:759697 CAPLUS
DN 128:60291
TI Neuronal histamine deficit in Alzheimer's disease
AU Panula, P.; Rinne, J.; Kuokkanen, K.; Eriksson, K. S.; Sallmen, T.; Kalimo, H.; Relja, M.
CS Department of Biology, Abo Akademi University, Turku, FIN-20520, Finland
SO Neuroscience (Oxford) (1997), Volume Date 1998, 82(4), 993-997
CODEN: NRSCDN; ISSN: 0306-4522
PB Elsevier Science Ltd.
DT Journal
LA English
AB Histamine is known to be a neurotransmitter in the brain, but it has not been clearly implicated in major diseases. All histaminergic neurons reside in the posterior hypothalamus and innervate most brain areas, which is compatible with the concept that histamine is involved in general central regulatory mechanisms. A sensitive, high-performance liq. chromatog. fluorimetric method was used to measure histamine contents in post mortem Alzheimer brains and age-matched controls. The cellular storage sites and distribution of histaminergic nerve fibers were examd. with a specific immunohistochem. method. The histamine content was reduced in the hypothalamus (42% of control value), hippocampus (43%) and temporal cortex (53%) of Alzheimer brains. Differences in other cortical areas, putamen, and substantia nigra were not significant. Histamine-contg. nerve fibers were found in the hippocampus, parahippocampal gyrus, and subiculum of both Alzheimer brains and controls. No histamine-contg. mast cells were seen in these temporal structures. Histamine in the human temporal lobe is stored in nerve fibers originating from the posterior hypothalamus, and not in mast cells. Decrease in brain histamine may contribute to the cognitive decline in Alzheimer's disease directly or through the cholinergic system. Development of drugs that penetrate the blood-brain barrier and increase histaminergic activity might be beneficial in Alzheimer's disease.

AN 1997:110225 CAPLUS
DN 126:223838
TI Similar deficits of central histaminergic system in patients with Down syndrome and Alzheimer disease
AU Schneider, Christoph; Risser, Daniele; Kirchner, Liselotte; Kitzmueller, Erwin; Cairns, Nigel; Prast, Helmut; Singewald, Nicolas; Lubec, Gert
CS Department of Pediatrics, University of Vienna, A 1090, Vienna, Austria
SO Neuroscience Letters (1997), 222(3), 183-186
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier
DT Journal
LA English
AB To study whether Alzheimer-like neuropathol. changes involve the central histaminergic system, the authors measured the concn. of histamine, its precursor histidine, and the activities of histidine decarboxylase (HDC) and histamine N-methyltransferase (HMT) in frontal cortex of aging Down syndrome (DS) patients, Alzheimer patients, and control individuals. The study populations were also investigated for choline acetyltransferase (ChAT) activity, since reduced ChAT activity is an established biochem. hallmark in DS and Alzheimer disease (AD). HDC and ChAT activity were reduced in brains of both DS and Alzheimer patients vs. control patients. Addnl., the authors obsd. a significant decrease of histamine levels in the DS group. Histamine levels in AD brains tended to be decreased. Histidine concns. and HMT activities were comparable between the three groups. Thus, the authors' results for the first time show histaminergic deficits in brains of patients with DS resembling the neurochem. pattern in AD. Neuropathol. changes may be responsible for similar neurochem. alterations of the histaminergic system in both dementing disorders.